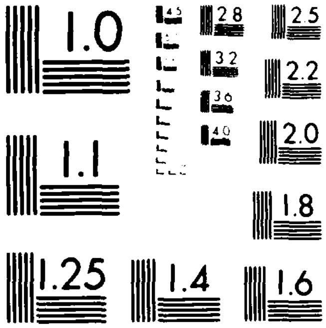
AD-A186 225 EVIDENCE FOR HUMAN ADAPTIVE RESPONSE TO DEHYDRATION: INCREASE OF CIRCULATING PROTEIN MASS(U) ARMY RESEARCH INST OF ENVIRONMENTAL MEDICINE NATICK MA 1/1

UNCLASSIFIED M N SAWKA ET AL. JUN 87 F/G 6/10 NL



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EVIDENCE FOR HUMAN ADAPTIVE RESPONSE TO DEHYDRATION: INCREASE OF CIRCULATING PROTEIN MASS

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Unclassified

SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

Form Approved OMB No. 0704-0188

1a. REPORT SECURITY CLASSIFICATION
Unclassified

1b. RESTRICTIVE MARKINGS

2a. SECURITY CLASSIFICATION AUTHORITY

2b. DECLASSIFICATION / DOWNGRADING SCHEDULE

3. DISTRIBUTION / AVAILABILITY OF REPORT
Approved for public release; distribution is unlimited

4. PERFORMING ORGANIZATION REPORT NUMBER(S)

5. MONITORING ORGANIZATION REPORT NUMBER(S)

6a. NAME OF PERFORMING ORGANIZATION
U.S. Army Res Inst of Env Med

6b. OFFICE SYMBOL (If applicable)

7a. NAME OF MONITORING ORGANIZATION

6c. ADDRESS (City, State, and ZIP Code)
Kansas Street
Natick, MA 01760-5007

7b. ADDRESS (City, State, and ZIP Code)
Kansas Street
Natick, MA 01760-5007

8a. NAME OF FUNDING / SPONSORING ORGANIZATION
Same as 6.a.

8b. OFFICE SYMBOL (If applicable)

9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER

8c. ADDRESS (City, State, and ZIP Code)

10. SOURCE OF FUNDING NUMBERS

PROGRAM ELEMENT NO.	PROJECT NO.	TASK NO.	WORK UNIT ACCESSION NO.
	3E162777 A879	879/BD	127

11. TITLE (Include Security Classification)
(U) Evidence for Human Adaptive Response to Dehydration: Increase of Total Circulating Protein Mass

12. PERSONAL AUTHOR(S) Michael N. Sawka, Ph.D., and C. Bruce Wenger, M.D., Ph.D.

13a. TYPE OF REPORT
Manuscript

13b. TIME COVERED
FROM ________ TO ______

14. DATE OF REPORT (Year, Month, Day)
June 1987

15. PAGE COUNT
7

16. SUPPLEMENTARY NOTATION

17. COSATI CODES

FIELD	GROUP	SUB-GROUP

18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
Dehydration; Plasma proteins; Human adaptation; Heat Stress

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

Previously, it was believed that humans do not adapt to dehydration. Data are presented here showing that within 15 hours after dehydration is reached, humans increase circulating protein mass to facilitate the redistribution of body water from the interstitial to the intravascular space. The increased resting circulating protein mass may also provide an advantage during situations in which dehydrated individuals have difficulty retaining their circulating protein, such as exercise in the heat.

20. DISTRIBUTION / AVAILABILITY OF ABSTRACT
☒ UNCLASSIFIED/UNLIMITED ☐ SAME AS RPT. ☐ DTIC USERS

21. ABSTRACT SECURITY CLASSIFICATION

22a. NAME OF RESPONSIBLE INDIVIDUAL
Michael N. Sawka, Ph.D.

22b. TELEPHONE (Include Area Code)
617-651-5141

22c. OFFICE SYMBOL
SGRD-UE-MEP

DD Form 1473, JUN 86 Previous editions are obsolete. SECURITY CLASSIFICATION OF THIS PAGE

Previously, it was believed that humans do not adapt to dehydration. Data are presented here showing that within 15 hours after dehydration is reached, humans increase circulating protein mass to facilitate the redistribution of body water from the interstitial to the intravascular space. The increased resting circulating protein mass may also provide an advantage during situations in which dehydrated individuals have difficulty retaining their circulating protein, such as exercise in the heat.

Dehydration, or a body water deficit, reduces man's ability to perform physical work as well as to survive in hot environments (1,2). A primary physiological mechanism mediating the adverse effects is that reduction of plasma volume below a certain level impairs the ability of the cardiovascular system to *simultaneously perfuse* metabolically active tissues and support the thermoregulatory requirements for heat loss. If an individual incurs a water deficit, hypovolemia will occur (1,2,3), and plasma volume can be defended only by a redistribution of body water. Plasma proteins, which do not readily pass through the capillary membrane, exert a plasma colloid osmotic pressure that favors redistribution of body water from the interstitial to the intravascular space.

It is generally believed that man does not adapt to dehydration (1,2). Recently, however, we noted a tendency for increased circulating protein mass (the product of plasma volume times plasma protein concentration) in several subjects resting in a comfortable environment ~15 h after an exercise-heat induced dehydration (4). This observation raised the possibility that dehydrated humans can acutely increase their circulating protein mass as an adaptation to redistribute body water to the intravascular space. To address this possibility, data from different dehydration experiments conducted over the past five years have been analyzed and presented.

Figure 1 shows individual data on the difference in resting circulating protein mass between euhydration and ~15 hours post-dehydration. Dehydration was achieved with restriction of food and fluid combined with exercise in the heat. After being dehydrated, subjects spent an equilibration period of ~15 hours (while maintaining the desired dehydration level) resting in a comfortable environment in which the hematological measurements were obtained. To control for the effects of previous exercise-heat stress, the euhydration measurements were obtained after an identical program of exercise-heat exposure (but with full fluid replacement) and the ~15 hour equilibration period.

Note that after ~15 hours of equilibration following dehydration, the resting circulating protein mass is usually increased above euhydration levels. There is no clear relationship between the magnitude of protein increase and the level of body water loss, but the largest increases of circulating protein mass occur with greater than an eight percent reduction in body water. The physiological stimulus for the increased resting circulating protein mass is unclear. Perhaps the protein increments are stimulated by the magnitude of plasma volume reduction (hypovolemia) during the dehydration process. Unfortunately, we did not quantitate the hypovolemia until ~15 hours after achievement of the dehydration level, when the adaptive processes had already occurred. All of these human subjects were previously heat acclimated, so it is unknown whether this adaptation occurs in unacclimated subjects also.

Several investigators have recently reported that dehydration elevates circulating protein mass in both rats (5) and baboons (6). Hemorrhage, an acute hypovolemic stress similar to dehydration, also elevates circulating protein mass in dogs (7). A common observation in all of these animal studies was an acutely increased hepatic albumin synthesis (5,6,7) and a reduced vascular permeability to albumin (5,6). Whether or not circulating protein mass is increased in

dehydrated humans by the same mechanisms needs to be investigated. Another possibility is an improved translocation of protein from the interstitial space and lymph to plasma during severe dehydration, perhaps employing parallel communications between the lymph nodes and venules (8,9).

The increased resting circulating protein mass may provide a reserve during situations where dehydrated individuals have difficulty retaining intravascular protein and therefore plasma. For example, if subjects are dehydrated, and then perform treadmill exercise in the heat while dehydrated, they frequently undergo a loss of circulating protein mass (and consequently of plasma volume) during the treadmill exercise (4,10). [In contrast, euhydrated subjects consistently add to their circulating protein mass, and hemodilute during treadmill exercise in the heat (4,10,11).] Likewise, Harrison (3) has found that during cycle exercise in the heat, subjects have a greater efflux of plasma protein when dehydrated than when euhydrated. Therefore, the increase in circulating protein mass at rest is an adaptive response that not only supports the circulation at rest, but also provides the dehydrated individual with a greater amount of intravascular protein as a reserve against conditions in which plasma protein is not easily retained.

In summary, in heat-acclimated humans dehydration elicits an adaptive increase of resting circulating protein mass, which helps translocate fluid from the interstitial to the intravascular space. This increase in circulating protein mass may also provide an advantage during situations in which dehydrated individuals have difficulty maintaining their circulating protein mass, such as exercise in the heat.

The views, opinions and/or findings in this report are those of the authors and should not be construed as official Department of the Army position, policy or decision unless so designated by other official documentation. Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Regulation 70-25 on Use of Volunteers in Research.

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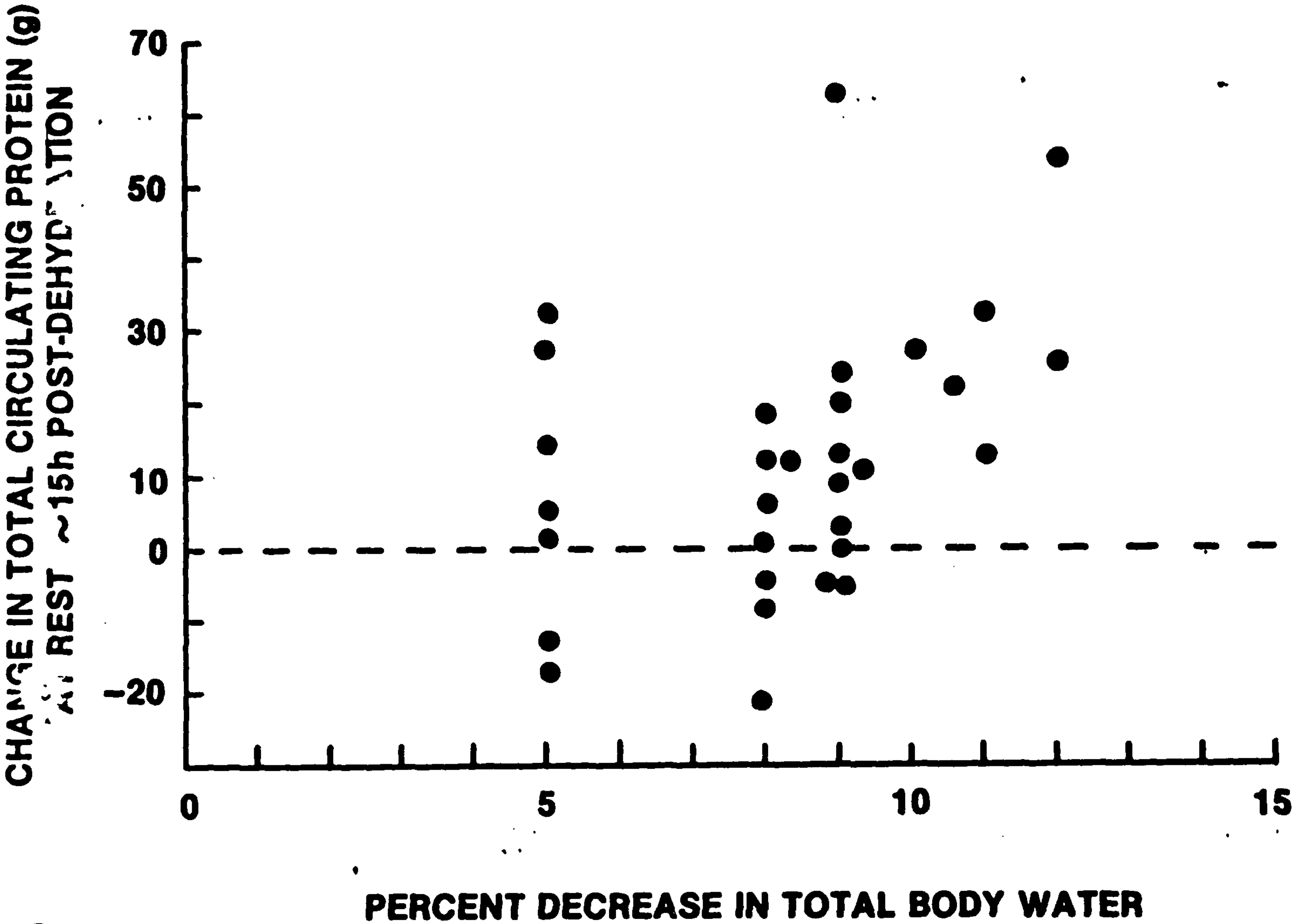
Fig. 1. Individual data for the change of resting circulating protein mass produced by dehydration. Dehydration was achieved with food and fluid ...ction combined with exercise in the heat. After being dehydrated, the subjects rested in a comfortable environment for ~15 hours while maintaining the desired dehydration level. The dotted line represents each subject's total circulating protein when euhydrated, from which changes were calculated.


CHANGE IN TOTAL CIRCULATING PROTEIN (g)
REST ~15h POST-DEHYD TION
70
50
30
10
0
-20
0
5
10
15
PERCENT DECREASE IN TOTAL BODY WATER

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